

10,626.445

03.11-05
PATENT

DOCKET NO.: JJPR-0032 (ORT-1377 DIV1)
Application No.: 10/626,445
Office Action Dated: November 8, 2004

Amendments to the Specification:

On page 1, following the title, please replace the paragraph with the following amended paragraph:

-- **CROSS-REFERENCE TO RELATED APPLICATIONS**

This is a divisional of U.S. Patent Application Serial Number 09/790,849, filed February 22, 2001, now pending abandoned, which claims benefit of U.S. Provisional Application Serial No. 60/208,260, filed May 31, 2000, now expired, the contents of both applications being incorporated in their entireties herein by reference. --

Please replace the paragraph at page 11, lines 10-27, with the following amended paragraph:

-- To determine the mammalian histamine H4 receptor DNA sequence(s) that yields optimal levels of mammalian histamine H4 receptor activity and/or mammalian histamine H4 receptor protein, human histamine H4 receptor DNA molecules including, but not limited to, the following can be constructed: the full-length open reading frame of the human histamine H4 receptor cDNA encoding the 44,495 kDa Daltons protein from approximately base 1 to base 1173 (these numbers correspond to first nucleotide of first methionine and last nucleotide before the first stop codon) and several constructs containing portions of the cDNA encoding human histamine H4 receptor protein. All constructs can be designed to contain none, all or portions of the 5' or the 3' untranslated region of human histamine H4 receptor cDNA. Human histamine H4 receptor activity and levels of protein expression can be determined following the introduction, both singly and in combination, of these constructs into appropriate host cells. Following determination of the mammalian histamine H4 receptor DNA cassette yielding optimal expression in transient assays, the mammalian histamine H4 receptor DNA construct is transferred to a variety of expression vectors, for expression in host cells including, but not limited to, mammalian cells, baculovirus-infected insect cells, E. coli, and the yeast S. cerevisiae. --

Please replace the paragraph at page 3, lines 3-18, with the following amended paragraph:

BRIEF DESCRIPTION OF THE DRAWING DRAWINGS

Figure 1 - The complete nucleotide coding sequence of human histamine H4 receptor (SEQ ID NO: 1) including untranslated regions is shown.

Figure 2 - The amino acid sequence of human histamine H4 receptor (SEQ ID NO: 2) is shown.

Figure 3 - The tissue distribution of the human histamine H4 receptor is shown.

Figure 4 - Binding of [³H]-histamine to the human H4 receptor is shown.

Figure 5 Panels A, B and C – The complete nucleotide coding sequence of mouse (A), guinea pig (B), and rat (C) histamine H4 receptors is shown.

Figure 6 Panels A, B and C – The amino acid sequence of mouse (A) (SEQ ID NO: 5), guinea pig (B) (SEQ ID NO: 7), and rat (C) (SEQ ID NO: 6) histamine H4 receptors is shown.

Figure 7 – The alignment of the polynucleotide sequences of the human, guinea pig, mouse and rat histamine H4 receptor is shown.

Figure 8 – The alignment of the polypeptide sequences of the human, guinea pig (SEQ ID NO: 10), mouse (SEQ ID NO: 8) and rat (SEQ ID NO: 9) histamine H4 receptor is shown.

Please replace the paragraph at page 40, lines 8-10, with the following amended paragraph:

EXAMPLE 4 EXAMPLE 2

Cloning of human histamine H4 receptor cDNA into a Mammalian Expression Vector

Please replace the paragraph at page 43, lines 10-11, with the following amended paragraph:

EXAMPLE 5 EXAMPLE 3

Binding assay on recombinant human histamine H4 receptor

Please replace the paragraph at page 44, lines 5-6, with the following amended paragraph:

~~EXAMPLE 6~~ EXAMPLE 4

Primary Structure Of The human histamine H4 receptor Protein

Please replace the paragraph at page 45, lines 11-12, with the following amended paragraph:

~~EXAMPLE 7~~ EXAMPLE 5

Cloning of the human histamine H4 receptor cDNA into E. coli Expression Vectors

Please replace the paragraph at page 46, lines 5-7, with the following amended paragraph:

~~EXAMPLE 8~~ EXAMPLE 6

Cloning of human histamine H4 receptor cDNA into a Baculovirus Expression Vector for Expression in Insect Cells

Please replace the paragraph at page 47, lines 5-6, with the following amended paragraph:

~~EXAMPLE 9~~ EXAMPLE 7

Cloning of human histamine H4 receptor cDNA into a yeast expression vector

Please replace the paragraph at page 48, line 1, with the following amended paragraph:

~~EXAMPLE 10~~ EXAMPLE 8 – Cloning murine, rat, and guinea pig histamine H4 receptor cDNAs

Please replace the paragraph at page 51, line 3, with the following amended paragraph:

~~EXAMPLE 11~~ EXAMPLE 9 – Ligand binding to mammalian histamine H4 receptors.

Please replace the paragraph at page 52, lines 3-4, with the following amended paragraph:

~~EXAMPLE 12~~ EXAMPLE 10

RT-PCR detection of human H4 mRNA expression.

Please replace the paragraph at page 53, lines 9-11, with the following amended paragraph:

Clark, M. A., A. Korte, et al. (1993). "Guanine nucleotides and pertussis toxin reduce the affinity of histamine H4 H3 receptors on AtT-20 cells." Agents Actions **40**(3-4): 129-34.

Please replace the paragraph at page 39, lines 7-6, with the following amended paragraph:

-- A histamine H4 receptor probe was generated by polymerase chain reaction using the following primer pair. 5' oligo: 5'
ACTAGAATTCACCGTGATGCCAGATACTAATAGCACA 3' [SEQ.ID. NO.: 1] and 3' oligo: 5' ATGCAGGATCCAGCATTTGAGACTGACAGGTAT 3' [SEQ.ID.NO.: 2].
The final probe sequence is shown in Figure 6. Amplification was cycled 35 times with a 50-60°C annealing temperature and human thalamus cDNA as template. The PCR fragment that was generated (400-500 bp) was 32P-labelled using the klenow fragment of DNA polymerase I and an oligo-labeling kit (Pharmacia). The fragment was then cleaned by one passage through a S-200 column (Pharmacia). --